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# Precursor Chemicals Trends: U.S. Perspectives

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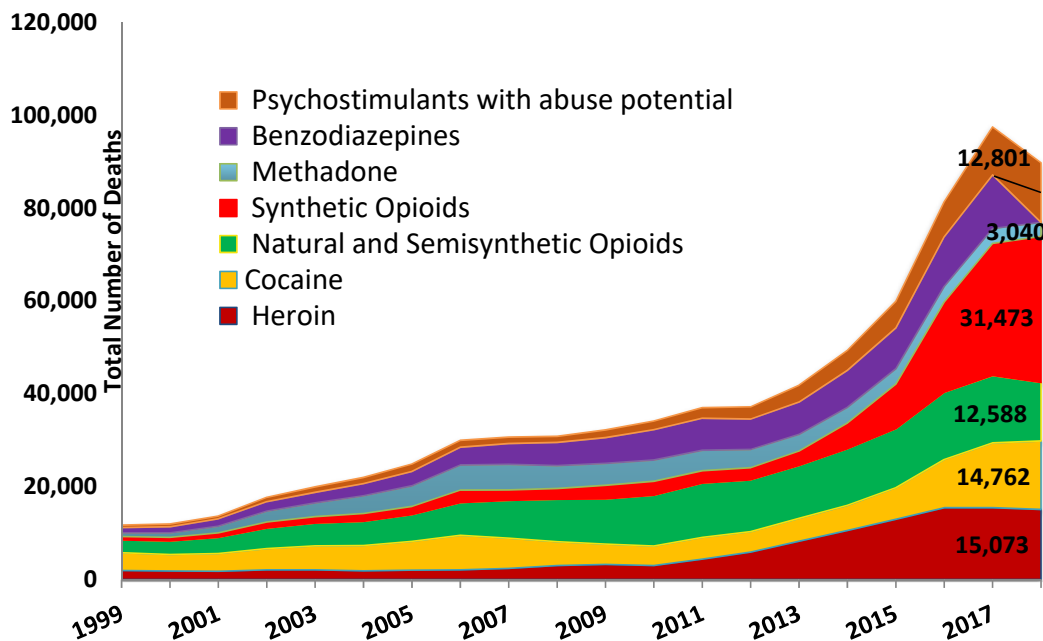
Diversion Control Division

United States Drug Enforcement Administration

# Opioid Health Crisis

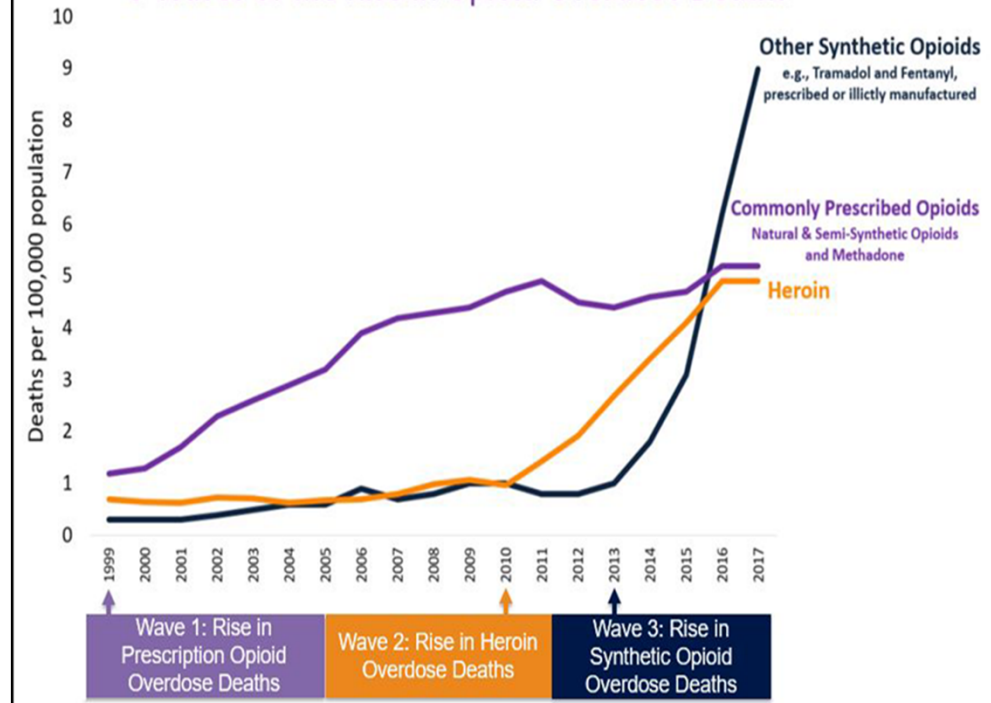


Total Number of Overdose Deaths, 1999 - 2018

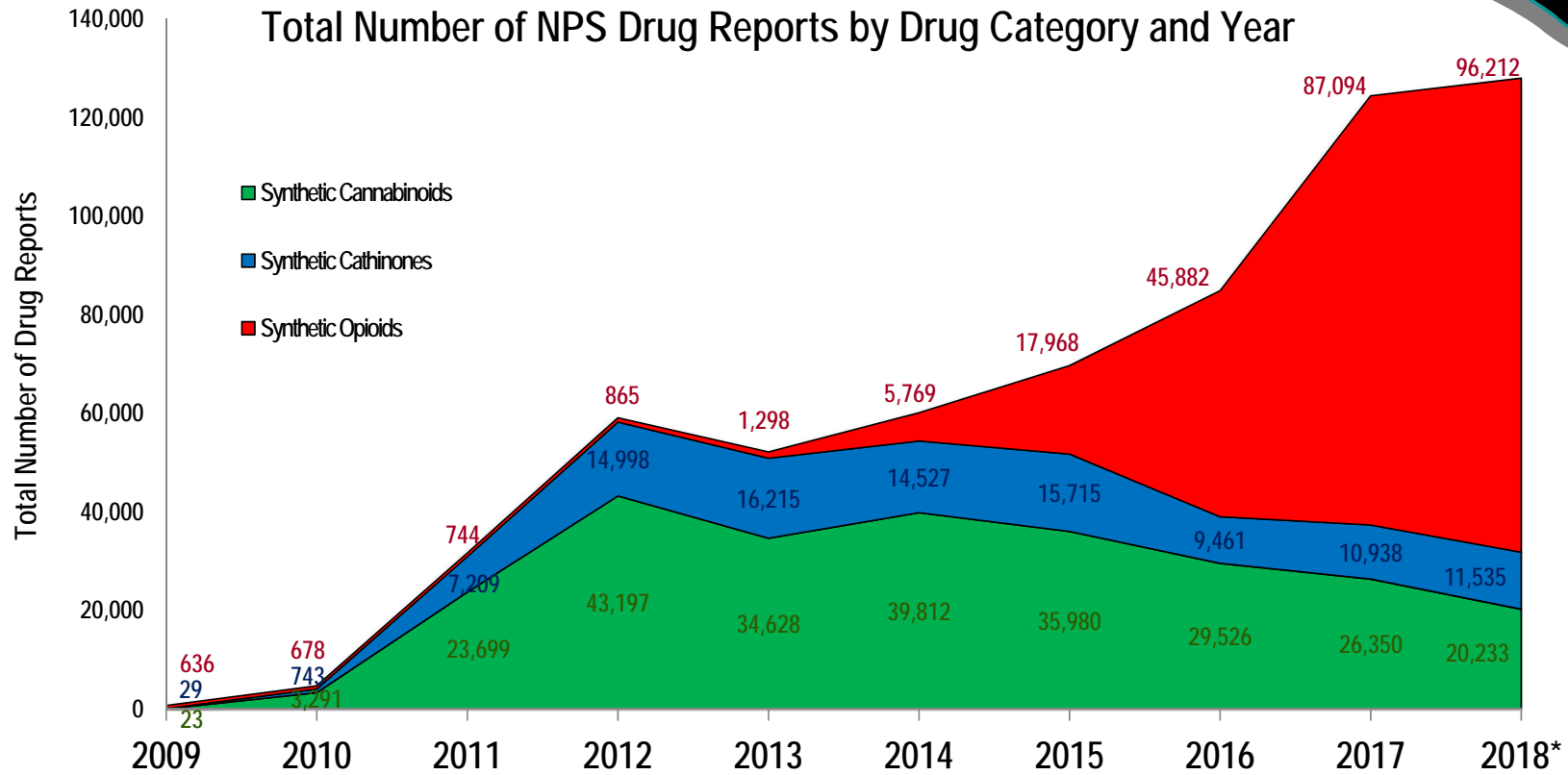


--- 2018 Provisional data (12-Month Period Ending on December 2018)  
No provisional data for benzodiazepine drug class

3 Waves of the Rise in Opioid Overdose Deaths

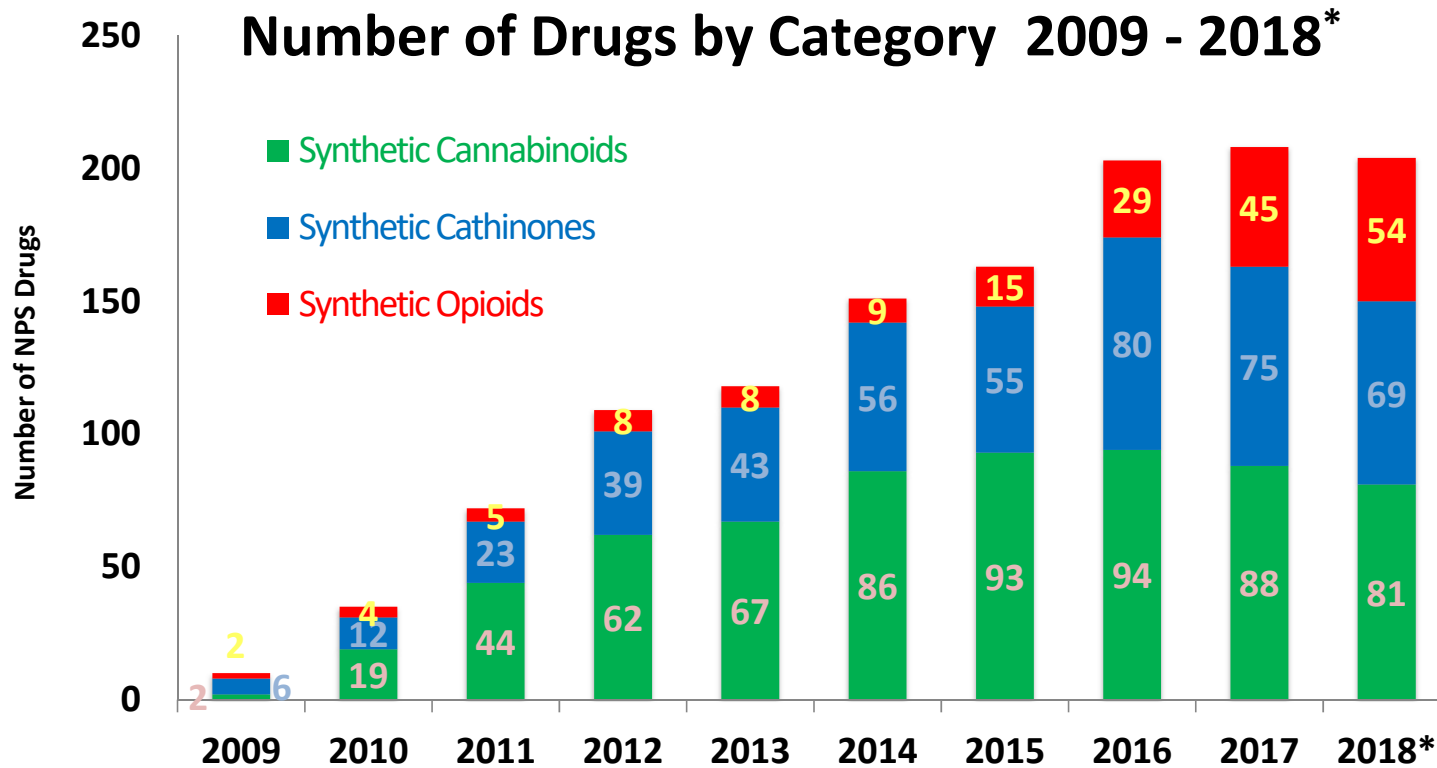


# Number of NPS Encounters in U.S.



Source: National Forensic Laboratory Information System (NFLIS), DEA, Queried as of June 12, 2019. \* NFLIS reporting still pending.

# Number of NPS in U.S.



\* NFLIS reporting still pending.

Source: National Forensic Laboratory Information System (NFLIS), DOE/DC/DEA, Queried as of June 12, 2019

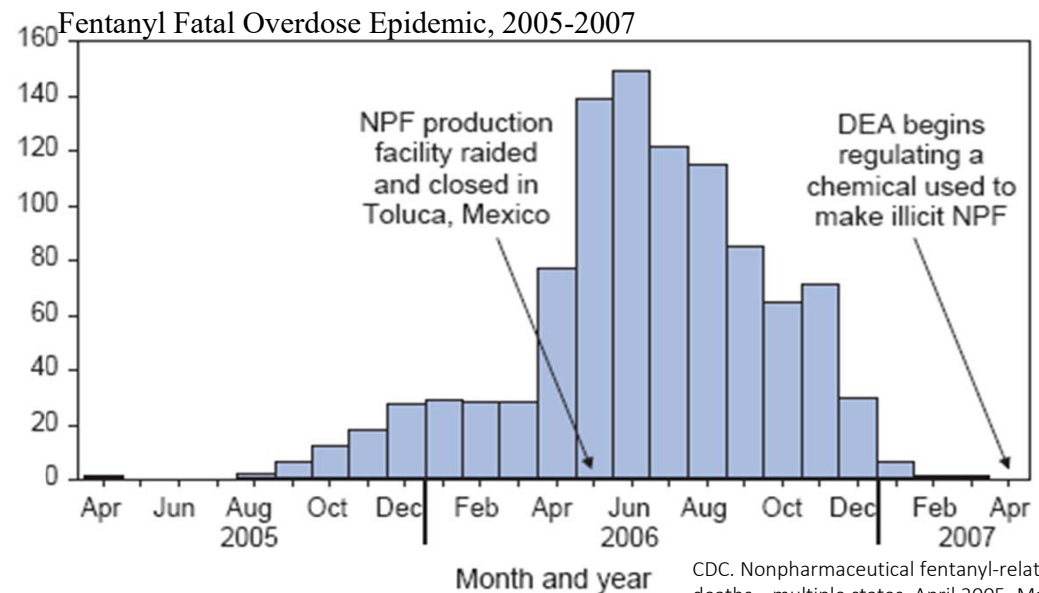


# Fentanyl Clandestine Laboratory -2006



- April 2005 - March 2007: Spike in fentanyl seizures
- Over 1013 documented non-pharmaceutical (NPF) overdose deaths
- Primary synthetic route identified as Siegfried method

- *N*-phenethyl-4-piperidone (NPP) added as a List 1 chemical in 2007
- 4-anilino-*N*-phenethyl-4-piperidine (ANPP) added as a Schedule II immediate precursor in 2010



CDC. Nonpharmaceutical fentanyl-related deaths—multiple states, April 2005–March 2007. MMWR 2008; 57: 793–6.



Administration

# Fentanyl Clandestine Laboratory - 2016



\* EVERYTHING DRY & ARGON

ANPP + TEA + DCM 1oz  
 DRY FLASK, STIR UNDER ARGON 10M  
 1/2 H  
 TRANSFER PROPANOL CE TO  
 ADDIN FUNNEL FOR SOME DRY BEN  
 TO THIS TO DRY

4-ANPP 41.2g → 70 → 103.15g  
 TEA 21.2ml → 36ml → 53.0m  
 DCM 100ml → 750-1000ml → 1850m  
 PECL  
 PECL 200ml → 45.5 → 107ml  
 44.2

ANPP 125g 14g  
 TEA 109g 7ml  
 DCM 1850ml 900ml  
 PECL 100ml 9.1 PECL

0°-5° C  
 AFTER  
 1M

BEAMS  
 10 MIN  
 BELOW  
 TO 146  
 P/WISE,  
 DCM  
 5MIP

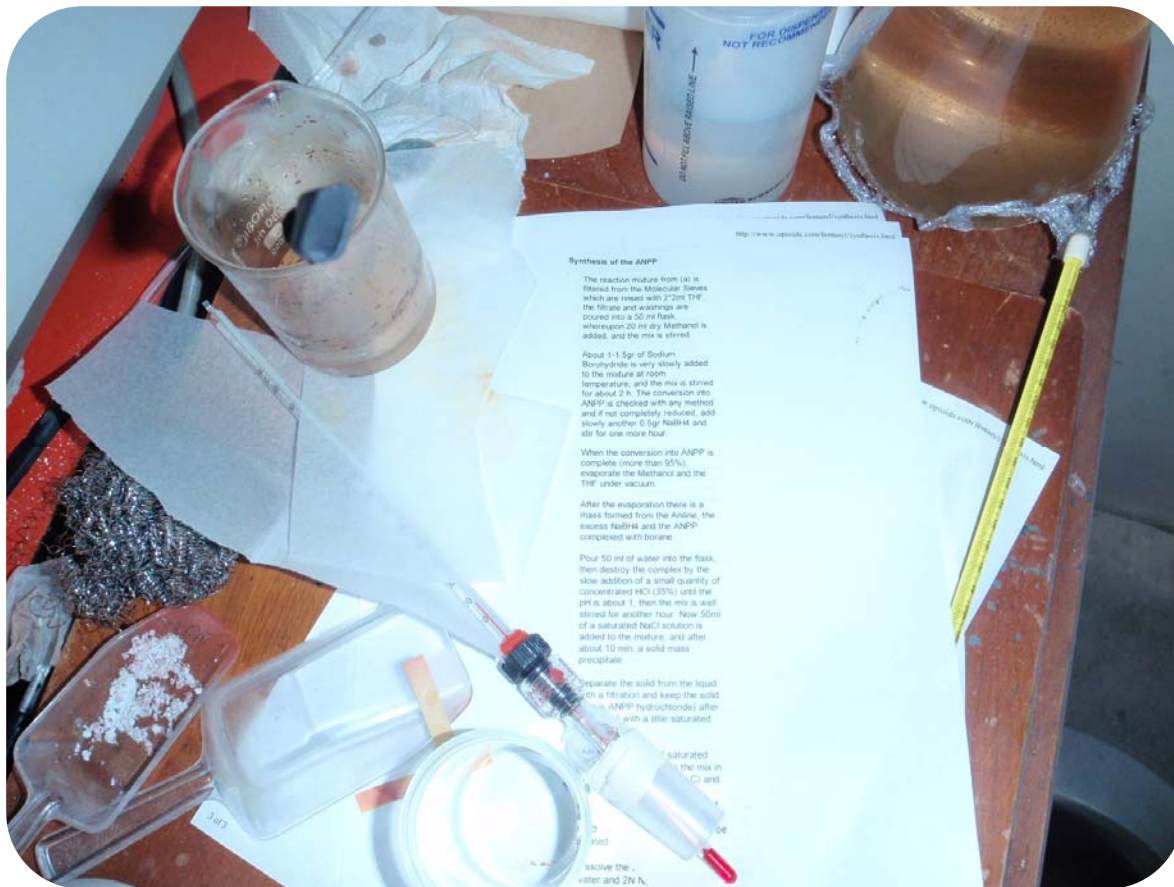
ANPP/4-  
 ANPP



# Clandestine Pill Press Operation



# Fentanyl Synthesis - Siegfried Route



<http://www.opioids.com/fentanyl/synt>

## Synthesis of the ANPP

The reaction mixture from (a) is filtered from the Molecular Sieves which are rinsed with 2\*2ml THF, the filtrate and washings are poured into a 50 ml flask, whereupon 20 ml dry Methanol is added, and the mix is stirred.

About 1-1.5gr of Sodium Borohydride is very slowly added to the mixture at room temperature, and the mix is stirred for about 2 h. The conversion into ANPP is checked with any method and if not completely reduced, add slowly another 0.5gr NaBH4 and stir for one more hour.

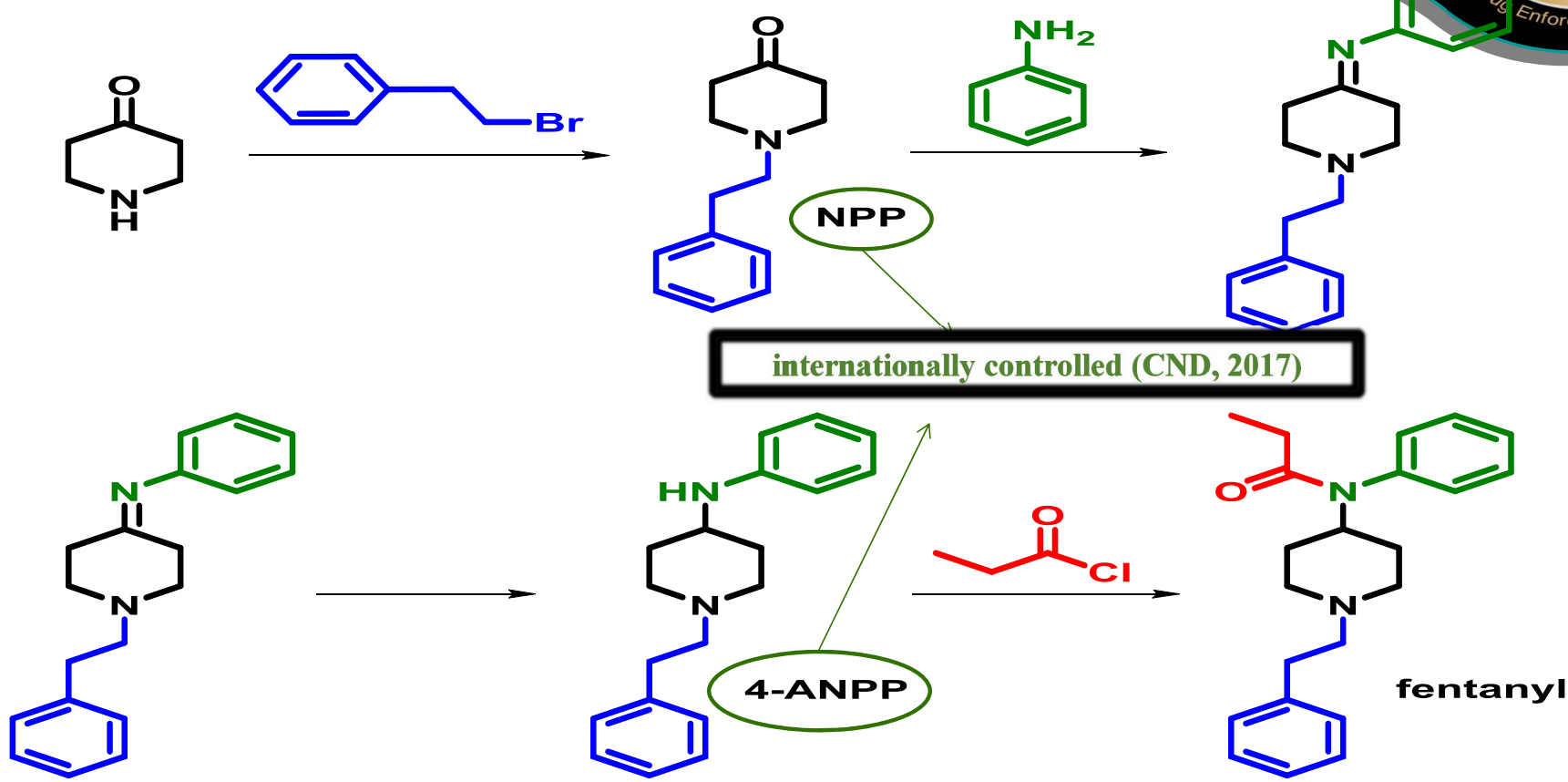
When the conversion into ANPP is complete (more than 95%),



# Synthetic Opioids in Counterfeit Tablets



# Control of Precursor Chemicals



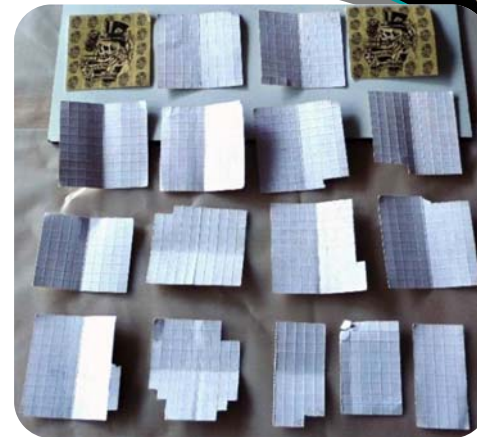
# Variety of Delivery Methods



cyclopropyl  
fentanyl spray



aerosolized acetyl



carfentanil on blotter paper

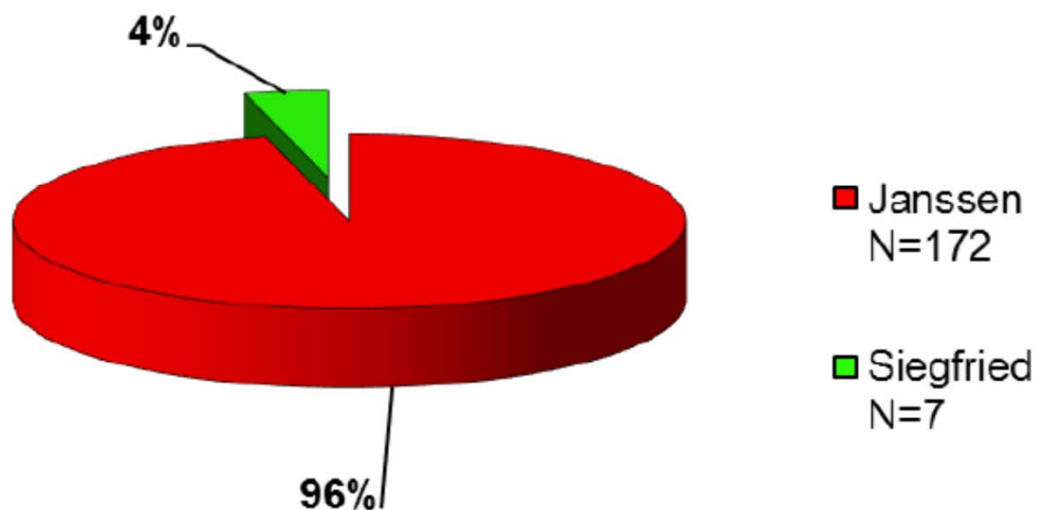


deceased tested  
positive  
for acetyl fentanyl

# U.S. Fentanyl Signature and Profiling Program



## Synthetic Route Determined for Fentanyl Seized in CY 2018

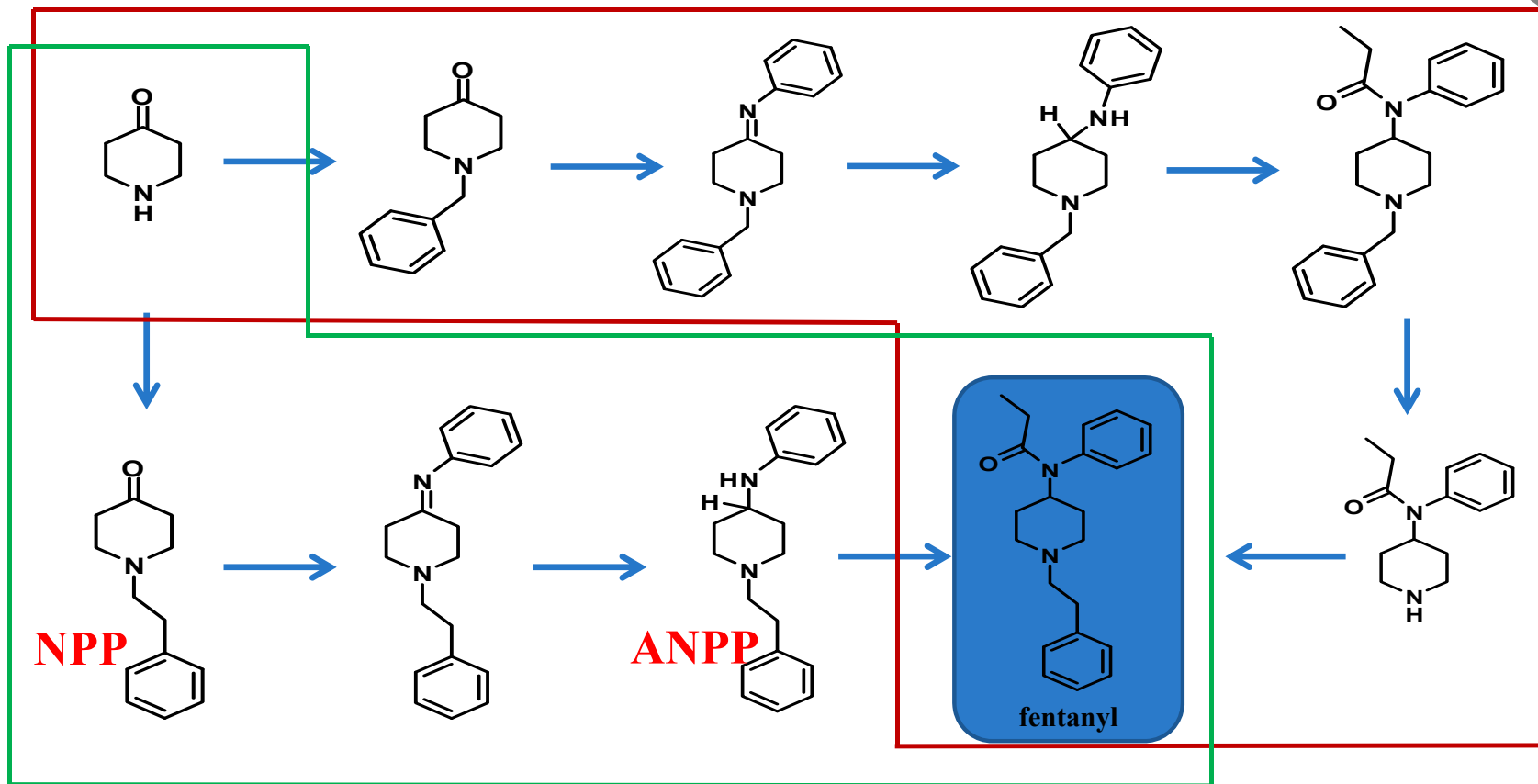




# Analysis of Fentanyl Synthesis



Janssen



NPP

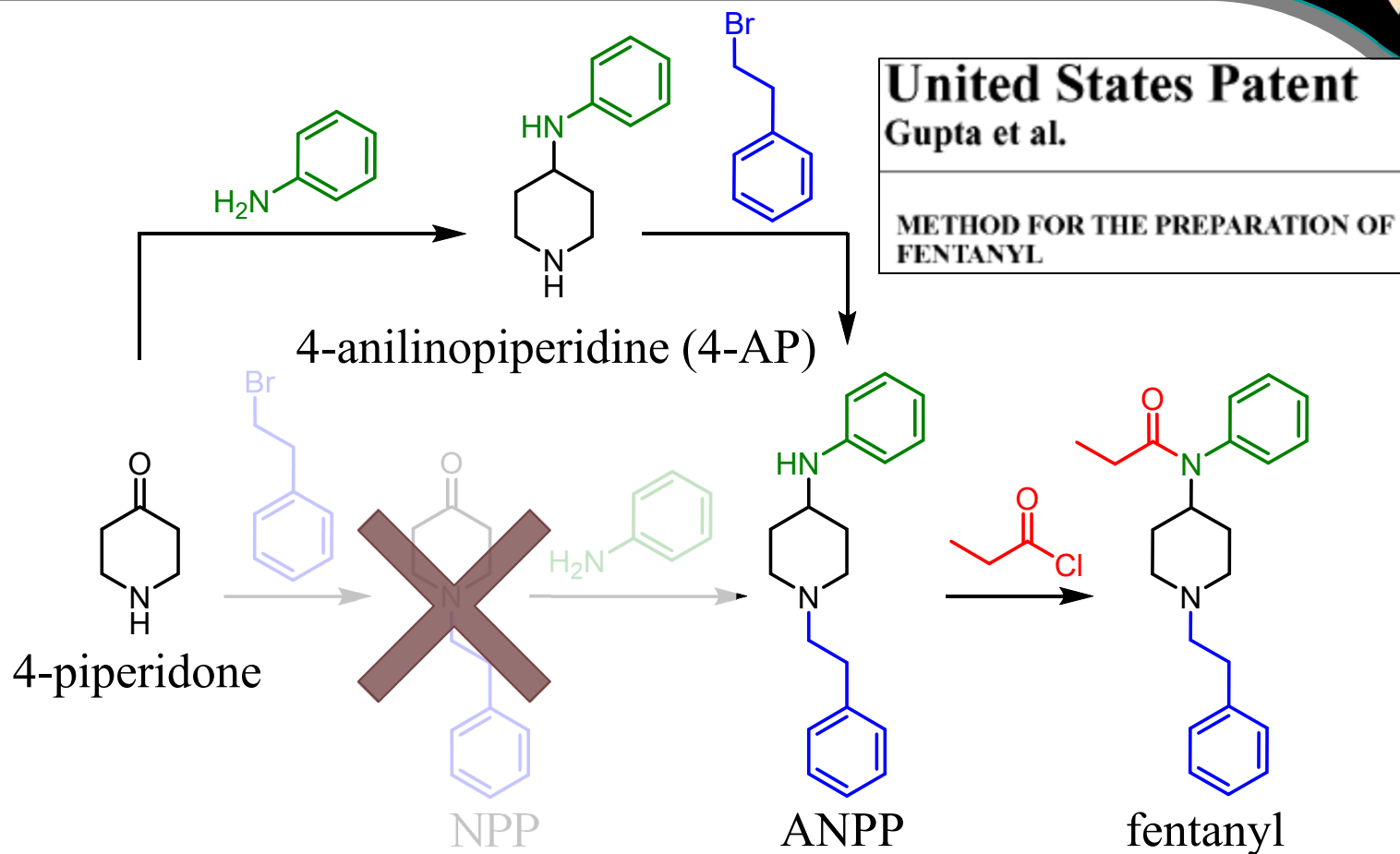
ANPP

fentanyl

Diversion Control Division

Siegfried

# Fentanyl Synthesis - Other Methods



# Fentanyl Synthesis – New Precursors



- New method utilizes a substance called **4-AP** instead of NPP
- INCB reported 32 notifications (late 2018 - early 2019) representing **30 kg of 4-AP**
- Origins: China, Hong Kong, Netherlands, Singapore, India
- Destination: Mexico

30 kg of 4-AP can produce 57 kg of fentanyl!



Picture 1+2 (© PGR Mexico)



Country of origin: China  
Goods declared: snacks

falsely declared as “foodstuffs or consumables”, “gifts”, “unspecified goods”, “glass bottles” and “protein”

# Fentanyl Precursor - Packaging



Picture 9 (© PGR Mexico)  
Country of origin: Singapore  
Goods declared: gift



Picture 10 (© PGR Mexico)  
Country of origin: Netherlands  
Goods declared: glass bottles



Picture 12 (© PGR Mexico)  
Country of origin: China  
Goods declared: n/a



Picture 14 (© PGR Mexico)  
Country of origin: China  
Goods declared: protein

# Suppliers Help to Evade Customs Detection



“discreet package :the packing suits you best would be chosen to **cross customs safely**. or if you have **your own ideal way**, it could be also taken into consideration .”

“safety guarantee (we do this business long time ,we **know how to disguise let the product through customs**)”

“our company promise to deliver clients' package to his hands safely, or we'll **cover the total loss and reship** in time”



Customer feedback that the 99918-43-1 with high quality and perfect packaging (+86 18034552304)

11 views

👍 0 🗨️ 0 ➦ SHARE ⌵ SAVE ...

Cathy Han

Published on May 24, 2019

SUBSCRIBE 1

CAS 99918-43-1, CAS 62-44-2 Phenacetin, bmk glycidate CAS 37148-48-4, CAS 37148-47-3, CAS 99-92-3 4-Aminoacetophenone, CAS 40064-34-4 4-Piperidone Hydrochloride Monohydrate, CAS 103-81-1, 2-Phenylacetamide, CAS 13605-48-6, PMK powder, CAS 103-63-9, (2-Bromoethyl)benzene, CAS 2f-dck, 5fadB, NDH, HGH

Whatsapp :008618034552304

Skype:cathy@hbhuanhao.com

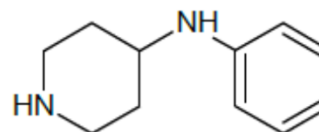
Hebei Huanhao Biotechnology co., Ltd.

# Precursor Chemical Names



*N*-Phenyl-4-piperidinamine is also known under the following common synonyms (list not exhaustive):

- *N*-Phenylpiperidin-4-amine
- 4-Anilinopiperidine
- 4-AP
- Despropionyl norfentanyl
- Piperidine, 4-anilino-
- 4-Piperidinamine, *N*-phenyl-
- CAS registry number [23056-29-3](#)

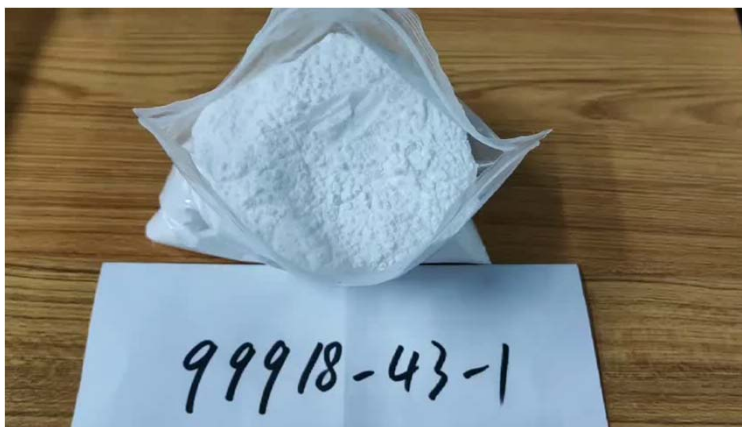


From a January 2019 International Alert

	Salt form	CAS number
	Base	<a href="#">23056-29-3</a>
	Hydrochloride (1:1)	1193388-65-6
	Hydrobromide (1:1)	24775-80-2
	Hydrobromide (1:2)	24998-99-0
	4-methylbenzenesulfonate (1:?)	918535-64-5
	Hydrochloride (1:2)	99918-43-1

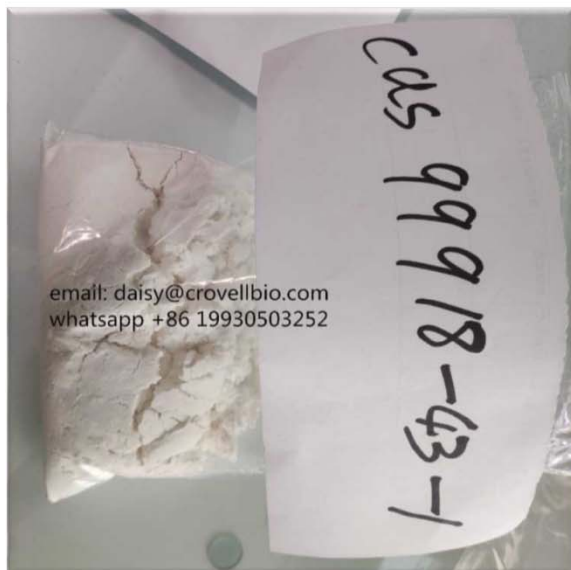


# Precursor Chemical – CAS Numbers



Salt form	CAS number
Base	23056-29-3
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Hydrobromide (1:1)	24775-80-2
Hydrobromide (1:2)	24998-99-0
4-methylbenzenesulfonate (1:?)	918535-64-5
Hydrochloride (1:2)	99918-43-1

# Internet Sales - Precursor Chemicals



email: daisy@crovellbio.com  
whatsapp +86 19930503252

**Trade Lead** Views: 82

**daisylang**  
**Hebei Guanlang Biotechnology Co., Ltd**

Dec 11 2018

★★★★★  
Login to Rate Seller

031166562153  
031166562153  
[My Other Trade Leads](#)  
City: shijiazhuang  
Country: China  
Trade Specialty: Manufacturer  
Industry Category: Chemicals & Plastics

**N-PHENYLPYPERIDIN-4-AMINE DIHYDROCHLORIDE**

N-PHENYLPYPERIDIN-4-AMINE DIHYDROCHLORIDE CAS 99918-43-1 (daisy@crovellbio.com Factory supply 99% 4-Anilinopiperidine powder, CAS: 99918-43-1 **Fentanyl Intermediates** 4-Anilinopiperidine (hydrochloride) China supplier, hot selling N-Phenylpiperidin-4-Amine Dihydrochloride in stock Email daisy@crovellbio.com Factory supply 99% 4-Anilinopiperidine powder, CAS: 99918-43-1 Molecular Formula C17H21N3Cl Pharmaceutical PackAge 200g/200ml

in 250kgs plastic drum, 20mts/201cl Purity 99% min Storage stay in dry, cool and well-sealed Contact me if you need order the 99918-43-1 Email daisy@crovellbio.com whatsapp +86 19930503252

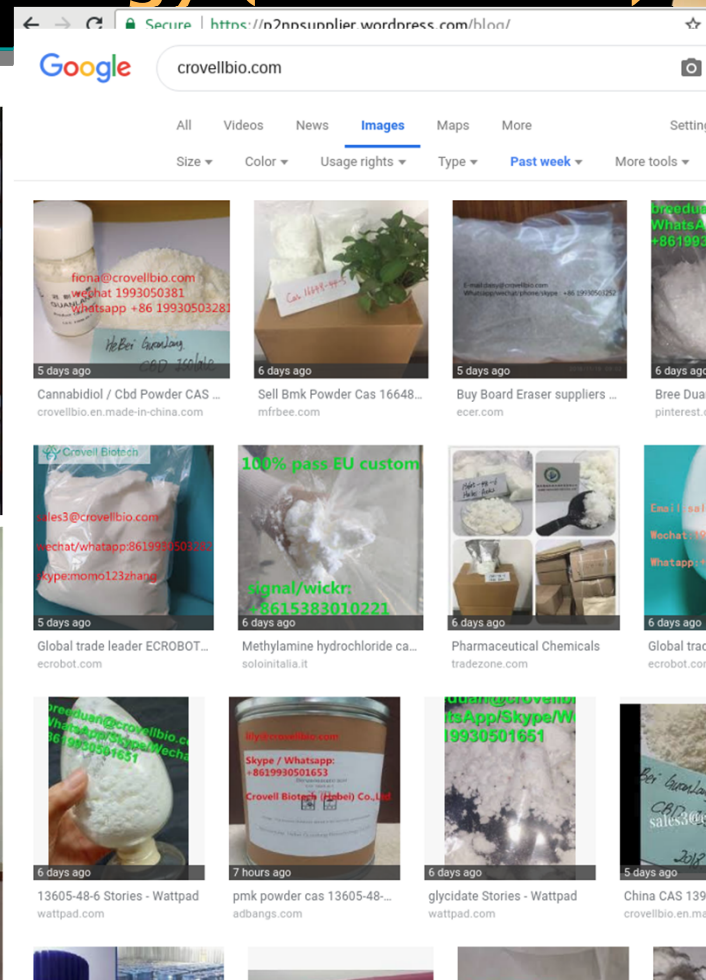
Diversion Control Division



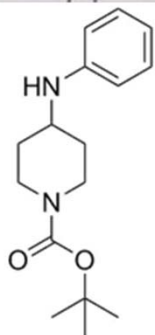
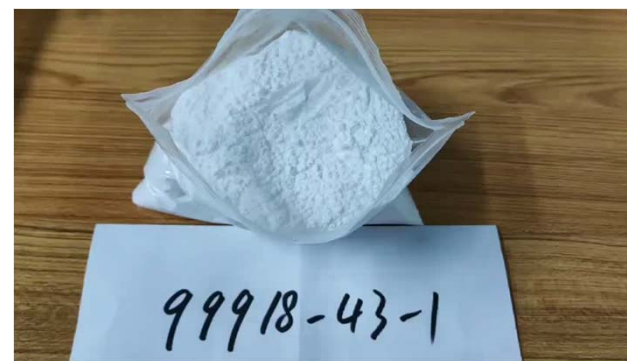
# Heibe Guanlang Biotechnology (Crovellbio)



- All products have a connection to drug trade
  - Designer precursors
  - Cutting agents
  - Non-controlled solvents
- Product offerings evolve re:
  - chemical controls
  - Pervasive online presence
  - Marking materials reference a “Mexico Branch”
  - Only one of many of examples



# Designer Precursor Chemicals

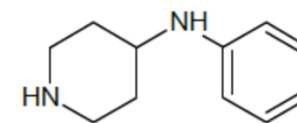


tert-butyl 4-(phenylamino)piperidine-1-carboxylate

CAS number: **125541-22-2**

*N*-Phenyl-4-piperidinamine is also known under the following common synonyms (list not exhaustive):

- *N*-Phenylpiperidin-4-amine
- 4-Anilinopiperidine
- 4-AP
- Despropionyl norfentanyl
- Piperidine, 4-anilino-
- 4-Piperidinamine, *N*-phenyl-
- CAS registry number: 23056-29-3



# Masked Precursor

factory supply

tert butyl

n boc

carboxylate cas

piperidine

piperidine cas

piperidine 125541

anilinopiperidine

cas 40064



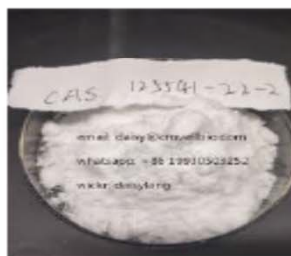
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wattpad.com



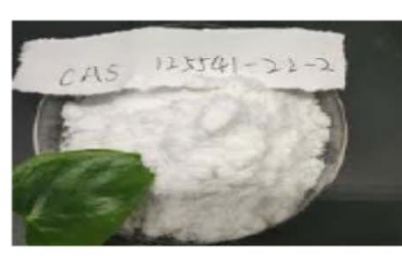
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cas 125541-22-2 - sop...  
wattpad.com



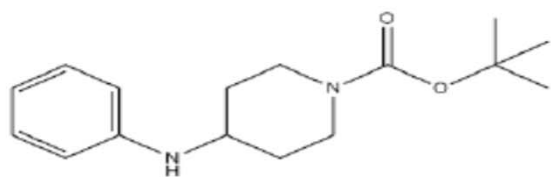
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China Factory Supply 1-N-Boc-4 ...  
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CAS 125541-22-2 tert-Butyl ...  
jamdeal.com



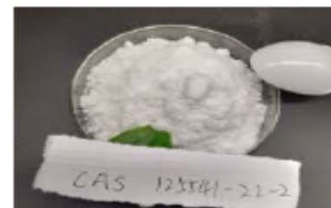
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802846.jumoreglobal.com



Piperidine CAS 125541-2...  
jamdeal.com



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putfree.com



N-Boc-4- (Phenylamino) Piperi...  
crovellbio.en.made-in-china.com



1-Boc-4-(Phenylamino)Piperidine ...  
putfree.com



125541-22-2 CAS# 125541-22-2 fact...  
jamdeal.com



tert-Butyl 4-anilinopiperi...  
wattpad.com



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crovellbio.en.made-in-china.com



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putfree.com



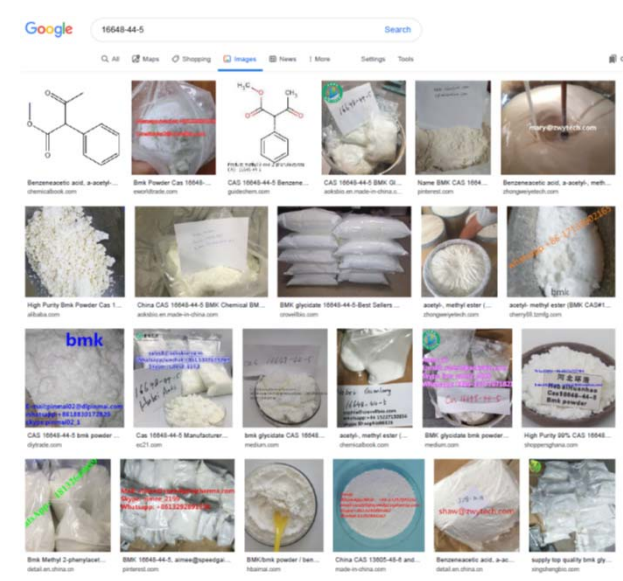
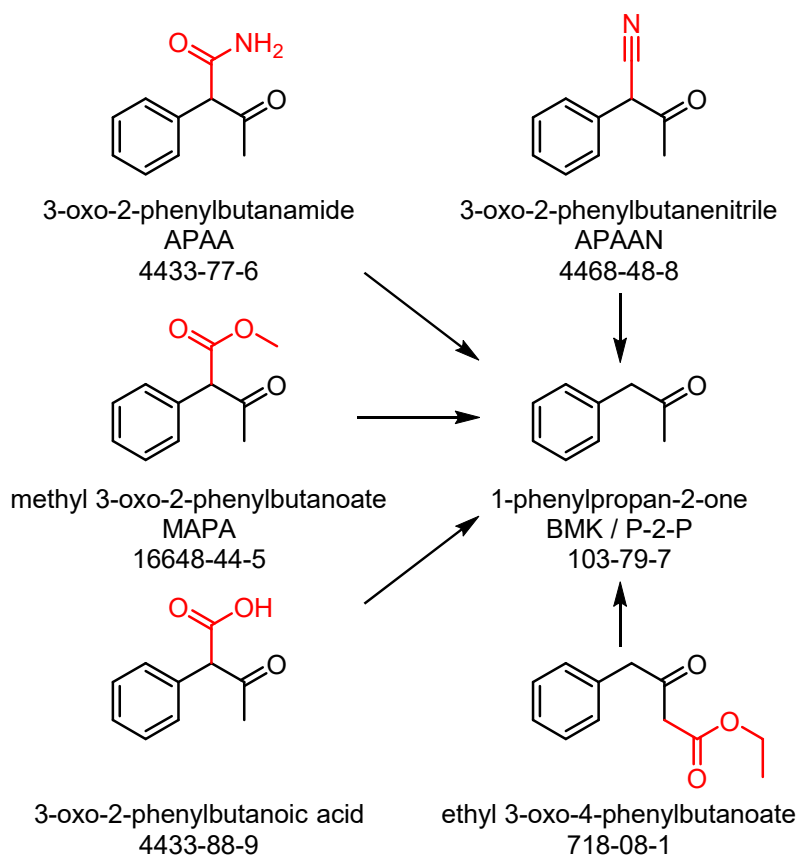
CAS No.125541-22-2,1 ...  
lookchem.com



# Methamphetamine Designer Precursor Chemicals



**MAPA**  
*methyl 3-oxo-2-phenylbutanoate*  
*methyl alpha-acetylphenylacetate*  
**CAS 16648-44-5**



# INCB on “Designer” Precursor Chemicals



**“designer” precursor:** A close chemical relative of a controlled precursor that is purpose-made to circumvent controls and usually does not have any recognized legitimate use.

- ❑ Established in 2013, in response to the proliferation of “designer” precursors
- ❑ The list currently contains 53 individual substances
- ❑ Expanded the list in a generic manner
- ❑ ISSL and definitions cover:
  - ✓ esters and other simple derivatives
  - ✓ Stable chemical intermediates,
  - ✓ Purpose-made chemical intermediates
  - ✓ Masked derivatives of controlled precursors
  - ✓ others

## Part 7. Non-Scheduled Chemicals

Recommendation	Reference (source)
The Board encourages Governments to ensure that mechanisms are in place to record information on all chemicals found to be used in the illicit manufacture of drugs and not only those scheduled under the 1988 Convention.	(PRE/2004/P83)
INCB wishes to remind Governments of the importance of sharing information about non-scheduled chemicals, their sources, the modus operandi of traffickers and the actual or suspected use of non-scheduled chemicals in illicit drug manufacture. Such information-sharing should start at the national level, when a company receives a suspicious order and reports it to the competent national authorities; and such information should also be shared at the international level, to prevent traffickers from exploiting weak links elsewhere. PICS provides an opportunity for the early sharing of such information worldwide.	(PRE/2015/P102) (PRE/2014/P155) (PRE/2013/P123) (PRE/2012/P159) (PRE/2006/P26)
When substitute chemicals are identified (stopped or seized) in international trade, it is important to communicate widely the reasons why the shipment was stopped or seized so as to alert the relevant authorities — nationally and globally — so that they can identify future shipments routed through different border crossings, ports or countries. Similarly, detailed information on seizures of substitute chemicals in illicit laboratories provides an opportunity for follow-up investigations, identifying those involved and preventing future diversions. The Board therefore urges all Governments to improve the extent, frequency and level of detail of shared information, also in relation to non-scheduled chemicals.	(PRE/2012/P94) (PRE/2012/P159)
Noting similarities in current issues related to precursors and to new psychoactive substances, the Board calls for urgent practical measures to effectively prevent and counter this new and dangerous trend and recommends that Governments support the development of adequate multilateral mechanisms to communicate to INCB incidents involving new psychoactive substances and products containing them, with a view to establishing or confirming emerging trends and contributing to devising early countermeasures.	(AR/2013/R12)
The Board encourages Governments to put in place effective mechanisms for identifying and investigating suspicious transactions involving such non-scheduled substances.	(AR/2007/R18) (PRE/2008/P94) (PRE/2007/P32) (PRE/2007/P89)
The Board wishes to remind Governments that communicating incidents involving new substances that have not previously been encountered in a given jurisdiction may help to establish or confirm new trends and may contribute to the development of countermeasures. Early communication of information about a suspicious shipment or of concerns about a shipment is critical in that it alerts the relevant authorities at the national and international levels so that similar shipments routed through different border crossings, ports or countries can be identified.	(PRE/2013/P151) (AR/2009/R36) (PRE/2005/P81)
All Governments are encouraged to make use of the Board's updated international special surveillance list of non-scheduled chemicals, which is available to competent national authorities.	(PRE/2009/P112) (PRE/2008/P94) (PRE/2007/P62) (PRE/2007/P89) (PRE/2003/P89)

# Contact Information



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**U.S. Drug Enforcement Administration**

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